1954-363
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	)	
	)	
Jerry L. NADLER et al.	)	
	)	
Serial No.: New- Div. of 08/945,744	)	Examiner: To Be Assigned
	)	
Filed: Herewith	)	Group Art Unit: To Be Assigned
	)	
For: HUMAN LEUKOCYTE 12-LIPOXYGENASE AND ITS ROLE IN THE PATHOGENESIS OF DISEASE STATES	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination on the merits, please amend the above-application as follows:

IN THE ABSTRACT:

Please insert the attached Abstract of the Disclosure filed herewith as the last page of this document.

IN THE SPECIFICATION:

Page 1, delete lines 4-9 and substitute therefore the following paragraph:

--This application is a divisional of U.S. Serial No. 08/945,744, filed November 3, 1997, which is a 371 of PCT/US96/06328, filed May 3, 1996, and a continuation-in-part of United States application Serial No. 08/434,681, filed May 4, 1995, which is a continuation-in-part of

PCT/US94/00089, filed January 4, 1994, which is a continuation-in-part of United States application Serial No. 07/936,660, filed August 28, 1992, now abandoned.--

Page 8, after line 33, please add the following paragraphs:

--Figure 8 is an immunoblot illustrating the dose-dependent effect of PDGF on UEGF expression in MCF-7 cells.

Figure 9 is an immunoblot showing the effect of EGF and 12-HETE on VEGF expression in MCF-7 cells.

Figure 10 is an immunoblot providing data on the effect of 12-HETE on VEGF expression in an immortalized human aortic smooth muscle cell line.

Figure 11 provides data on the effects of 12-LO products on DNA synthesis in RINm5F cells.

Figure 12 is a Western blot of proteins isolated from RINm5F cells showing the effect of IL-1β on 12-LO protein expression.

Figure 13 illustrates the effects of IL-1β on 12-HETE production in rat islets.

Figure 14A shows the effects of IL-1B on 12-LO mRNA expression in porcine aortic smooth muscle cells. Figures 14B and 14C show the same information for IL-4 and IL-8, respectively.

Figure 15 illustrates data on mRNA for the marker GAPDH.

Figure 16 illustrates the effect of IL-4 on leukocyte 12-LO protein expression in porcine vascular smooth muscle cells.

Figure 17 shows the same data as Figure 16 for IL-8.

Figure 18 provides data on the effect of IL-4 on 12-LO activity in porcine smooth muscle cells.

Figure 19 shows the same data as Figure 18 for IL-8.

Figure 20 illustrates data regarding the upregulation of human leukocyte 12-LO by IL-1, IL-4 and IL-8.

Figure 21 shows increases in 12-LO mRNA in the pancreatic islets of increasingly diabetic rats.

Figure 22 shows levels of 12-LO mRNA in diabetic and non-diabetic ZDF rats.

Figure 23 present data pertaining to rat fibroblasts overexpressing the human insulin receptor at different glucose concentrations in the presence or absence of baicalein.

Figure 24 shows data regarding the HETE/PGI_2 ratio in different diabetic groups.

Figure 25 provides data regarding Wistar and GK rats under Chow and Cafeteng diet conditions.

Figure 26 shows increased amounts of 12-LO in diabetic (GK) rats compared to normal (Wistar rats).

Figure 27 shows data demonstrating increase in phosphorylation of the insulin receptor β subunit by insulin as affected by 12-HETE.

Figure 28A shows glucose levels in rats fed a high fat diet versus a control diet. Figure 28B represents the area under the glucose-tolerance curve in Figure 28A for high fat fed rats and control rats.

Figure 29 illustrates JNK activity as a function of 12-HETE concentration.

Figure 30 is an immunoblot showing JAK1 and JAK2 bands under control and 10^{-7}M 12-HETE conditions.--

IN THE DRAWINGS:

Applicant is submitting herewith twenty-four (24) sheets of formal drawings. Please replace the twenty-three (23) sheets of informal drawings with the new formal drawings.

AFTER THE SPECIFICATION:

Please delete the Sequence Listing at pages 54-59 and substitute therefore the attached substitute Sequence Listing.

IN THE CLAIMS:

Please cancel claims 6-9, 22-27, 29-31, 33 and 37 without prejudice or disclaimer.

Claim 4, line 2, after "condition" insert a comma.

Please amend claim 32 as follows:

32. (Amended) A [The] method for treating a patient having a disease state in which 12-HETE is an etiological agent which comprises decreasing mitogenic activity in said patient [of claim 29], wherein the mitogenic activity is decreased by administering a therapeutically effective amount of a 12-LO inhibitor to said [the] patient sufficient to decrease mitogenic activity.

REMARKS

The present amendments to correct certain informalities in the application. In particular, the amendments correct the priority information cited in the specification and insert an Abstract of the Disclosure and provide a description of the drawings for Figures 8-30. The amendment to claim 32 is made to correct dependency of the amended claim on a claim which has been cancelled. The amendment inserts the language of cancelled claim 29 and does not contain any new matter.

In addition, a substitute sequence listing is provided in both computer readable form and paper copy. I hereby state that the information recorded in computer readable form is identical to the written sequence listing, and that the sequences contained in the sequence listing are supported in the application as filed. None of the amendments contain new matter.

Early and favorable allowance is earnestly solicited. Please charge any fee or credit any overpayment pursuant to 37 C.F.R. §1.17 to Deposit Account No. 02-2135.

Respectfully submitted,

By: _____

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